AMENDMENTS TO THE SPECIFICATION

Deletions are ~~strikethrough~~ and additions are underlined.

Paragraph [0010], last sentence

The Greek alphabets "alpha", "beta", "gamma" and "delta" refer to the degree of methyl substitutions in the chroman structure (Table 1).

Insert after paragraph [0010]

Table 1. Molecular weights

	Tocopherol	Tocotrienol
Alpha	430	424
Beta	417	411
Gamma	417	410
Delta	403	396

Vitamin E, including tocopherols and tocotrienols, are typically 390 - 430 Daltons in molecular weight or more broadly 350 - 450 Daltons in molecular weight, which includes tocopherols and tocotrienols without any methylated groups in the lower range and tocopherols and tocotrienols with fully methylated groups in the higher range.

Paragraph [0015]

Table ~~1~~ 2 shows a non-exhaustive sample of diverse health benefits and protection of the eight classically and individually known E vitamers. A need exists to develop a rationale for an "appropriate spectrum" tocols product that would normalize and/or optimize biologic functions without the crossover mitigation of tocopherols. To date, only "full spectrum" tocols (implied presence of all eight tocols) are commercially available, espousing to deliver the composite health benefits of the individualized effects of those found in Table ~~1~~ 2. It remains unsubstantiated that full-spectrum tocols will deliver the complete effects of these individually identified properties. Therefore, these full-spectrum tocols lack a compositional, technical and/or scientific basis or rationale. Currently, no present art teaches compositions and methods of use in humans, nor teaching so efficaciously and by simply adding natural tocols extracts in appropriate combinations.

Table ~~1~~ 2. Isolated uses and effects of individual tocopherols and tocotrienols.

Paragraph [0017]

Soy and corn oils contain exclusively tocopherols, although they tend to be highest in the C5 unsubstituted tocopherols (70-90% as delta-T1 and gamma-T1) (see, Sheppard, A. et al., 1993). Such high levels of C5 unsubstituted delta-T1 and gamma-T1 from soy and corn (Table ~~2~~ 3) have unique admixture application, which unexpectedly have not been implemented.

Table ~~2~~ 3. Compositional abundance of tocotrienols in various plant source materials.

Paragraph [0058]

In one embodiment the invention is drawn to a composition comprising annatto extract where the composition produces beneficial effects listed in Tables ~~1~~ 2 ~~& 3~~ 4. In a preferred embodiment the invention is drawn to a composition comprising annatto extract where C5 unsubstituted tocols produce the beneficial effects in Table s ~~1~~ 2 ~~& 3~~ 4.

Table ~~3~~ 4. Appropriate spectrum ~~tocos~~ tocols based on annatto ~~tocos~~ tocols and/or admixture applications.*

Paragraph [00127]

In one embodiment an appropriate spectrum composition with annatto tocols and extracts where the appropriate spectrum composition has applications described in Table ~~3~~ 4. In one embodiment TRF from palm and rice can be separated (e.g. chromatography) to fractionate or improve individual tocotrienols.

Paragraph [00139]

Table ~~4~~ 5 shows the effect of annatto tocotrienol on lipidemic subjects and how it affected the drop of total cholesterol, LDL, and triglycerides, as well as, increasing HDL over each of the first 3 months and through 12 months. The duration of the study was designed to correspond to standard procedures for managing lipids effectively in just one month from supplementation and lasting indefinitely with continued usage. The annatto tocotrienol dose

(about 50-100 mg per day) to reduce lipids was about two to three-fold less than other tocols materials (about 100-300 mg per day) typically from palm or rice TRFs. The significantly lower dose underscored the efficient bioavailability of the special C5 unsubstituted T3 unique to annatto extracts. The results were also applicable to C5 unsubstituted tocopherols, since gamma-T1 and delta-T1 are more bioavailable than C5 substituted tocopherols. Further, the lower dose of annatto tocotrienol in the human studies was due to a composite of other factors, specifically, it was a) mainly delta-T3 and gamma-T3, b) tocopherol-free, and c) delta-T3 and gamma-T3 behave synergistically. The TRFs in other sources contain large proportions of alpha-T3 which is the weakest (at least five-fold less active) cholesterol reducer and has no synergistic role with other tocotrienols.

Table ~~4~~ 5. Supplementation of annatto tocotrienols (75 mg per day) from 1 to 12 months on lipid reduction in lipidemic subjects.

Paragraph [00141]

Table ~~5~~ 6 compares the lipid management of normal weight and overweight/obese subjects. The cholesterol management (i.e., TC and LDL) improved in both groups and again triglycerides dropped in both groups. Generally, it is difficult to raise HDL in overweight subjects, and the increase in this group was modest (4%) compared to the normal weight group (10%). Nonetheless, the HDL increased with annatto tocotrienol supplementation. It was clearly documented that annatto extract tocotrienols effectively treated lipidemia of normal weight and overweight/obese subjects.

Table ~~5~~ 6. Supplementation of annatto tocotrienols on normal weight and overweight/obese lipidemic subjects*.

Paragraph [00142]

The insulin resistance criteria were assessed on humans supplemented with annatto tocotrienol (Table ~~6~~ 7). Both TG/HDL and TG dropped approximately 20-30% in normal weight subjects (2-month and 3-month studies) and in overweight/obese subjects (8-month study). Annatto C5 unsubstituted tocotrienols improved insulin sensitivity (IS) as evaluated by these two

surrogate markers. Typically 4 of 5 subjects in each group had improved TG and TG/HDL, which showed improved insulin sensitivity. Also, 50% of the subjects in all groups (Table ~~6~~ 7) that were previously IR prior to tocotrienol supplementation, based on the TG/HDL ratios, or about 20-40% reversal of IR back to IS if based on TG numbers, reversed back to IS.

Table ~~6~~ 7. Human supplementation of annatto tocotrienols on improvement of insulin sensitivity and reversal of insulin resistance (IR)*

Paragraph [00145]

Table ~~7~~ 8 shows a 20-50% drop in CRP of subjects taking annatto tocotrienols. This represented the first time that tocotrienols (from any source) effectively reduced CRP. Tocotrienols reduced inflammation processes, which was responsible for a more effective reduction of atherosclerosis and thrombosis than previously envisioned when measured simply by cholesterol-associated lipids alone. The combined effect of annatto tocotrienols more effectively lowered lipids and inflammation processes, managed atherosclerosis and IR together, rather than just hypercholesterolemia by itself. Tocopherol was known to lower CRP to a comparable range to the present work (Table ~~7~~ 8), but surprisingly, the required dosages of alpha-T1 are approximately 10-fold higher than that of annatto tocotrienols. This 10-fold potency of tocotrienols over tocopherol was due to the unique composition of C-5 unsubstituted tocotrienols.

Table ~~7~~ 8. Human supplementation of annatto tocotrienols (75 mg per day) from 1 to 3 months on cardiovascular inflammation (C-reactive protein) reduction.

Paragraph [00146]

There was a possible role of inflammatory proteins on the prediabetic condition, especially of IR, since people with IR have higher VCAM-1, CRP, IL-6 and TNFα. Since this study showed that annatto tocotrienols clearly lowered IR and CRP (Tables ~~5~~ 6 and ~~6~~ 7), it has been demonstrated that tocotrienols, especially C5 unsubstituted T3, help prevent diabetes and CVD (Figure 3 and Table ~~4~~ 5).

Paragraph [00147]

HDL increased (4 - 19%) in all subjects on annatto tocotrienol supplementation (Tables 4 5 and ~~5~~ 6), indicating a reduction in cardiovascular risk. The supplementation even raised HDL in overweight subjects. Therefore, the annatto C5 unsubstituted T3, via increased HDL, exerted marked anti-inflammatory and anti-thrombotic effects independent of CRP, and inhibited/suppressed chemotactic bioactive materials (CBM) that tether circulating cells to arteries, inhibited LDL oxidation and NFkB activation.